

WHAT IS CLAIMED IS:

1. A non-naturally-occurring polypeptide having an amino acid sequence sufficiently duplicative of that of naturally-occurring stem cell factor to allow possession of a hematopoietic biological activity of naturally occurring stem cell factor.
2. A purified polypeptide comprising naturally-occurring stem cell factor.
3. A polypeptide according to Claim 1 or 2 wherein said polypeptide is the product of prokaryotic or eukaryotic expression of an exogenous DNA sequence.
4. A polypeptide according to Claim 3 wherein said polypeptide is the product of CHO cell expression.
5. A polypeptide according to Claim 3 wherein the exogenous DNA sequence is a cDNA sequence.
6. A polypeptide according to Claim 1 or 2 wherein said stem cell factor is human stem cell factor.
7. A polypeptide according to Claim 3 wherein the exogenous DNA sequence is a genomic DNA sequence.
8. A polypeptide according to Claim 3 wherein the exogenous DNA sequence is carried on an autonomously replicating DNA plasmid or viral vector.

9. A polypeptide according to Claim 1 possessing part or all of the amino acid sequence of human stem cell factor as set forth in Figure 15B, Figure 15C, Figure 42 or Figure 44 or any naturally-
5 occurring allelic variant thereof.

10 10. A polypeptide according to Claim 1 which has an in vivo biological activity of naturally-
occurring stem cell factor.

11. A polypeptide according to Claim 1 which has an in vitro biological activity of naturally-
occurring stem cell factor.

15 12. A polypeptide according to Claim 1 or 2 further characterized by being covalently associated with a detectable label substance.

13. An isolated DNA sequence for use in
20 securing expression in a prokaryotic or eukaryotic host cell of a polypeptide product having an amino acid sequence sufficiently duplicative of that of naturally-
occurring stem cell factor to allow possession of a hematopoietic biological activity of naturally occurring
25 stem cell factor, said DNA sequence selected from among:

(a) DNA sequences set out in Figure 14B,
Figure 14C, Figure 15B, Figure 15C, Figure 42,
Figure 44, or their complementary strands;

30 (b) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and

(c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

14. A procaryotic or eukaryotic host cell transformed or transfected with a DNA sequence according to Claim 13 in a manner allowing the host cell to express said polypeptide product.

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15. A polypeptide product of the expression of a DNA sequence of Claim 13 in a procaryotic or eukaryotic host cell.

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16. An isolated DNA sequence coding for procaryotic or eukaryotic host expression of a polypeptide having an amino acid sequence sufficiently duplicative of that of naturally occurring stem cell factor to allow possession of a hematopoietic biological activity of naturally-occurring stem cell factor.

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17. A cDNA sequence according to Claim 16.

18. A genomic DNA sequence according to
20 Claim 16.

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19. A DNA sequence according to Claim 16 wherein said DNA sequence codes for human stem cell factor.

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20. A DNA sequence according to Claim 19 and including one or more codons preferred for expression in E. coli cells.

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21. A DNA sequence according to Claim 16 having the sequence set out in Figure 15B, Figure 15C, Figure 42 or Figure 44.

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22. A DNA sequence according to Claim 16 and including one or more codons preferred for expression in yeast cells.

23. A DNA sequence according to Claim 16
covalently associated with a detectable label substance.

24. A DNA sequence coding for a polypeptide
5 fragment or polypeptide analog of naturally-occurring
stem cell factor.

25. A DNA sequence as in Claim 24 coding for
methionyl stem cell factor.

10 26. A biologically functional plasmid or
viral DNA vector including a DNA sequence according to
Claim 16.

15 27. A procaryotic or eukaryotic host cell
stably transformed or transfected with a DNA vector
according to Claim 26.

20 28. A polypeptide product of the expression
in a procaryotic or eukaryotic host cell of a DNA
sequence according to Claim 16.

25 29. A polypeptide having part or all of the
amino acid sequence as set forth in Figure 15C,
Figure 42 or Figure 44 and having one or more of the
in vitro biological activities of naturally-occurring
stem cell factor.

30 30. A polypeptide having part or all of the
secondary conformation of naturally-occurring stem cell
factor and having part or all of the amino acid sequence
set forth in Figure 15C, Figure 42, or Figure 44 and
having a biological property of naturally-occurring
human stem cell factor.

31. A process for the production of stem cell factor comprising:

growing, under suitable nutrient conditions,
procaryotic or eukaryotic host cells transformed or
5 transfected with a DNA according to Claim 13, and
isolating desired polypeptide products of the
expression of DNA sequences in said vector.

32. A composition comprising a purified and
10 isolated human stem cell factor free of association with
any human protein in glycosylated or nonglycosylated
form.

33. A pharmaceutical composition comprising
15 an effective amount of a polypeptide according to
Claim 1 and a pharmaceutically-acceptable diluent,
adjuvant or carrier.

34. A method for treatment of leucopenia in a
20 mammal comprising administering a therapeutically
effective amount of the polypeptide according to
Claim 1.

35. A method for treatment of
25 thrombocytopenia in a mammal comprising administering a
therapeutically effective amount of the polypeptide
according to Claim 1.

30 36. A method for treating anemia in a mammal
comprising administering a therapeutically effective
amount of the polypeptide according to Claim 1.

37. A method for enhancing engraftment of
35 bone marrow during transplantation in a mammal
comprising administering a therapeutically effective
amount of the polypeptide according to Claim 1.

38. A method of enhancing bone marrow recovery in treatment of radiation, chemical, or chemotherapeutic induced bone marrow aplasia or myelosuppression which comprises treating patients with 5 therapeutically effective doses of stem cell factor.

39. A DNA sequence coding for an analog of human stem cell factor selected from the group consisting of:

10 a) $[\text{Met}^{-1}]$ stem cell factor; and
b) stem cell factor wherein one or more cysteines are replaced by alanine or serine.

40. A polypeptide product of the expression 15 in a prokaryotic or eukaryotic host cell of a DNA sequence according to Claim 39.

41. A pharmaceutical composition comprising recombinant stem cell factor having the human amino acid 20 sequence, and a pharmaceutically acceptable diluent, adjuvant or carrier.

42. An antibody specifically binding stem cell factor.

25 43. An antibody as in Claim 42 wherein said antibody is a monoclonal antibody.

44. A process for the efficient recovery of 30 stem cell factor from SCF containing material, the method comprising the step of subjecting the SCF containing material to ion exchange chromatographic separation.

45. A process as in Claim 44 wherein said ion exchange chromatographic separation is anion exchange chromatographic separation.

5 46. A process as in Claim 44 further comprising the step of reverse phase liquid chromatographic separation.

10 47. A process for the efficient recovery of stem cell factor from SCF containing material, the method comprising the step of subjecting the SCF containing material to reverse phase liquid chromatographic separation.

15 48. A polypeptide having the hematopoietic biological activity of naturally occurring stem cell factor, said polypeptide having an amino acid sequence set forth in Figure 15C, Figure 42 or Figure 44 or any allelic variants, derivatives, deletion analogs, 20 substitution analogs, or addition analogs thereof, and characterized by being the product of prokaryotic or eucaryotic expression of an exogenous DNA sequence.

49. A polypeptide as in Claim 48 selected 25 from the group consisting of:
SCF²-164, SCF⁵-164, SCF¹-130,
SCF¹-148, SCF¹-162, SCF¹-164, SCF¹-165, SCF¹-183
(Figure 15C); SCF¹-185, SCF¹-188, SCF¹-189, and SCF¹-248
(Figure 42); and SCF¹-157, SCF¹-160, SCF¹-161 and
30 SCF¹-220 (Figure 44).

50. A biologically active composition comprising the polypeptide of Claim 1 covalently attached to a water-soluble polymer.

51. A composition as in Claim 50 wherein
said polymer is selected from the group consisting of
polyethylene glycol or copolymers of polyethylene
glycol and polypropylene glycol, and said polymer is
5 unsubstituted or substituted at one end with an
alkyl group.

52. The composition of Claim 50 wherein the
polypeptide is [Met⁻¹] SCF1-164.

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53. The composition of Claim 50 wherein said
polymer has an average molecular weight of about 1,000
to 100,000 daltons.

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54. The composition of Claim 50 wherein said
polymer has an average molecular weight of about 4,000
to 40,000 daltons.

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55. The composition of Claim 50 wherein said
polymer is an unsubstituted polyethylene glycol or a
monomethoxy polyethylene glycol.

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56. The composition of Claim 50 wherein said
polymer is attached to said polypeptide via reaction
with an active ester of a carboxylic acid or carbonate
derivative of said polymer.

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57. The composition of Claim 50 wherein one
or more amino groups of said protein are conjugated to
said polymer by reaction with a N-hydroxysuccinimide,
p-nitrophenol or 1-hydroxy-2-nitro-benzene-4-sulfonate
ester of the polymer.

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58. The composition of Claim 50 wherein one
or more free cysteine sulfhydryl groups are conjugated
to said polymer via reaction with a mal imido or
haloacetyl derivative of the polymer.

59. The composition of Claim 50 wherein the polypeptide is glycosylated and the polymer is attached by reaction of an amino, hydrazine or hydrazone derivative of the polymer with one or more aldehyde groups generated by oxidation of the carbohydrate moieties.

60. A method for preparing a biologically active polymer-polypeptide adduct which comprises reacting the polypeptide of Claim 50 with a water-soluble polymer under conditions permitting the covalent attachment of the polymer to said polypeptide, and recovering the adduct so produced.

15 61. A method of treating acquired immune deficiency in a human comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

20 62. A method of treating neoplasia in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

25 63. A method as in Claim 62 wherein before said administering step is the step of administering chemotherapy or irradiation to said mammal.

30 64. A method of transfecting early hematopoietic progenitor cells with a gene comprising:
(i) culturing early hematopoietic progenitor cells with SCF; and
(ii) transfecting the cultured cells of step (i) with a gene.

65. A method of transferring a gene to a mammal comprising the steps of:

(i) culturing early hematopoietic progenitor cells with SCF;

5 (ii) transfected the cultured cells of step (i) with a gene; and

(iii) administering the transfected cells to said mammal.

10 66. A method of treating nerve damage in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

15 67. A method of treating infertility in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

20 68. A method of treating intestinal damage in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1.

25 69. A method of treating myeloproliferative disorder in a mammal comprising administering a therapeutically effective amount of the polypeptide according to Claim 1 conjugated to a toxin.

30 70. A polypeptide as in Claim 48 selected from the group consisting of:

$[\text{Met}^{-1}]SCF^1-148$, $[\text{Met}^{-1}]SCF^1-162$,

$[\text{Met}^{-1}]SCF^1-164$, $[\text{Met}^{-1}]SCF^1-165$, $[\text{Met}^{-1}]SCF^1-183$

(Figure 15C); $[\text{Met}^{-1}]SCF^1-185$, $[\text{Met}^{-1}]SCF^1-188$,

35 $[\text{Met}^{-1}]SCF^1-189$, and $[\text{Met}^{-1}]SCF^1-248$ (Figure 42); and $[\text{Met}^{-1}]SCF^1-157$, $[\text{Met}^{-1}]SCF^1-160$, $[\text{Met}^{-1}]SCF^1-161$ and $[\text{Met}^{-1}]SCF^1-220$ (Figure 44).